

Comparison of scoring systems' mortality prediction ability in COVID-19 intensive care patients over 80 years of age

Elderly mortality prediction in COVID-19

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Abstract

Aim: In this study, we aimed to compare the 30-day mortality prediction abilities of the acute physiology and chronic health evaluation II (APACHE II), CURB-65, pneumonia severity index (PSI), A-DROP, Infectious Diseases Society of America/American Thoracic Society severity criteria, and I-ROAD scores in patients aged over 80 years admitted to the intensive care unit with COVID-19 pneumonia.

Material and Methods: The study was conducted with a single-center retrospective observational design and included patients aged 80 years and older who were admitted to the intensive care unit due to COVID-19 pneumonia between March 2020 and August 2021. Patient demographic data, imaging findings, blood test results, discharge status, length of stay in the intensive care unit, duration of mechanical ventilation, inotropic drug administration status, presence/absence of mortality and vital signs at the time of admission were obtained from the hospital automation system. Then, the above-mentioned scores were calculated and compared statistically.

Results: The study was completed with 119 patients, 60 (50.4%) women and 59 (49.6%) men. The mean age of all patients was 84 (80-98) years, and the mortality rate was 84.03% (n=100). Among the scoring systems, I-ROAD had the highest area under the curve (AUC) value (0.703), APACHE II had the highest specificity (94%), and A-DROP had the highest sensitivity (64%).

Discussion: According to our results, the I-ROAD scoring system is an effective tool that can be used in the prediction of mortality related to COVID-19 pneumonia among intensive care patients aged ≥ 80 .

Keywords

Geriatrics, In-hospital Mortality, Scoring Systems, Mechanical Ventilation

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Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2, is a zoonosis with systemic involvement, especially affecting the respiratory system. The disease was first seen in Wuhan, China in December 2019 in the form of viral pneumonia and declared a pandemic by the World Health Organization on March 11, 2020. The clinical features of COVID-19 have been described in many epidemiological studies. Many studies have proven that advanced age is a risk factor for mortality in COVID-19 pneumonia [1,2]. Comorbid diseases have also been shown to be associated with mortality from COVID-19. In addition, it has been determined that approximately 19% of patients hospitalized due to COVID-19 have hypoxic respiratory failure and 12% require mechanical ventilation [1,3]. Intensive care is required in approximately 5-10% of patients, with the proportion being particularly higher in the elderly [4,5]. Intensive care is one of the most important steps in reducing mortality due to the COVID-19 pandemic.

Mortality in COVID-19 is mostly observed due to lung involvement and the associated acute respiratory distress syndrome (ARDS) that develops afterwards. In this sense, pneumonia severity scoring systems that have been used for many years can also be utilized in COVID-19 [6]. In addition, many different scoring systems have been developed in the fight against COVID-19 in order to predict mortality in the early and late stages of the disease [7].

Various organizations and associations across the world have developed pneumonia severity scoring systems, and there is ongoing debate on the use of such scoring systems in COVID-19 [6]. However, despite the availability of many different scoring systems for the prediction of mortality due to COVID-19, there is still no specific scoring system for the geriatric population, although the geriatric population constitutes the most risky group in terms of mortality [7]. If the mortality predictors of these patients can be better clarified, this could contribute to the fight against current and future pandemics. This will provide the use of optimal treatment modalities in these patients with a higher probability of mortality.

The primary objective of this study was to compare 30-day mortality prediction abilities of the CURB-65, pneumonia severity index (PSI), A-DROP, Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) criteria for severe community-acquired pneumonia, I-ROAD, acute physiology and chronic health evaluation II (APACHE II) scores in patients aged over 80 years followed up in the intensive care unit (ICU) with COVID-19 pneumonia [8,9]. The secondary objective was to determine the relationship of mortality with the patients' blood test results, mechanical ventilation duration, and comorbidities.

Material and Methods

This single-center, retrospective, observational, cohort study included patients aged over 80 years who were diagnosed with COVID-19 pneumonia from March 1, 2020, through August 1, 2021, and followed up and treated in the intensive care unit with the Z03 and sub-diagnosis codes according to the International Code of Disease, fourth edition. The study was approved by the ethics committee of Kartal Dr. Lutfi Kırdar City Hospital,

Health Science University (Decision number: 2021/514/208/17 Date:25/08/2021). The patients' epicrisis records were also screened. Parameters and scoring in the study were recorded in a digital data form. The complete case analysis method was used, and patients with missing data were excluded.

For all patients, age, gender, comorbidities, APACHE II, CURB-65, PSI, A-DROP, IDSA/ATS, and I-ROAD scores, white blood cell (WBC), neutrophil, lymphocyte, and platelet (PLT) counts, C-reactive protein (CRP), urea, creatinine, albumin, lactate dehydrogenase (LDH), sodium, potassium, and chlorine values, blood pressure, pulse, and body temperature values measured at the time of admission, blood gas parameters, namely pH, partial pressure of carbon dioxide (pCO_2), and bicarbonate (HCO_3), lactate values, base deficit levels, discharge status, length of ICU stay, duration of mechanical ventilation, inotropic drug administration status, presence/absence of in-hospital mortality, duration of treatment were obtained from the medical record system. Then, using these parameters, the following disease severity scores were calculated:

CURB-65: Confusion, urea > 7 mmol/L, respiratory rate ≥ 30 per minute, low blood pressure (systolic <90 mmHg or diastolic ≤ 60 mmHg), and age ≥ 65 years [1].

PSI: Pneumonia severity index [2].

A-DROP: Age >75 years in women and >70 years in men, blood urea nitrogen > 21 mg/dL or dehydration, $SaO_2 < 90\%$ or pCO_2 in blood gas < 60 mmHg, confusion, or systolic blood pressure < 90 mmHg [3].

IDSA/ATS: Infectious Diseases Society of America/American Thoracic Society [4].

I-ROAD: Immunodeficiency (malignant tumor or immunosuppressive condition), respiratory status [$SpO_2 > 90\%$ when the fraction of inspired oxygen (FIO_2) is $>35\%$], orientation (decreased state of consciousness), age (>70 years in men and >75 years in women), and dehydration [5].

The 30-day mortality prediction abilities of these scoring systems were compared.

Inclusion criteria

1. Age ≥ 80 years
2. Having been diagnosed with COVID-19 pneumonia confirmed by a positive reverse transcription-polymerase chain reaction test
3. Having been followed up and treated in the intensive care unit

Exclusion criteria

1. Age under 80 years
2. Incomplete treatment or follow-up
3. Incomplete or unavailable data

Sample Size

Using GPower 3.1 software package, the sample size required for the study was determined to be 112 in total for an 80% test power. The calculation was made by considering whether the continuous variables fit the normal distribution and tests that should be used in both cases. A total of 119 patients were included in the sample, and accordingly, the power of the test was calculated as 87.16%.

Statistical analysis

SPSS version 25 statistical package program was used for statistical analyses. The study data were summarized using

descriptive statistical methods (mean, median, frequency, percentage, minimum, and maximum). The Shapiro-Wilk test was used for the normality test of continuous variables. The Pearson chi-square test of independence was used for the independent testing of two categorical variables. To investigate differences between the two groups, the t-test was employed for continuous variables with a normal distribution, and the Mann-Whitney U test for non-normally distributed data. Two-by-two cross-tables were formed for classified variables, and their relationships were investigated with Fisher’s exact test. The significance level was taken as 0.05 for all tests.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

The data of a total of 119 patients, of which 60 (50.4%) were women and 59 (49.6%) were men, were included in the analysis. The mean age of all patients was 84 (80-98) years. Nineteen (15.96%) patients were discharged from the hospital, while mortality was observed in the remaining 100 (84.03%) patients. There was no statistically significant difference between the survivor and non-survivor groups in terms of body mass index, hypertension, diabetes mellitus, and cardiac, pulmonary, or neurological disease histories ($p > 0.05$). However, the mean length of ICU stay was significantly higher in the survivor group (44.05 days) compared to the non-survivor group (9.42 days) ($p = 0.036$). The mean duration of invasive mechanical ventilation (IVM) was 57.84 hours for the survivor group and 168.12 hours for the non-survivor group ($p = 0.00$), and the mean duration of non-invasive ventilation (NIV) was 41.74 and 2.22 hours, respectively ($p = 0.00$). Table 1 summarizes the laboratory results of the patients and the statistical comparison between the survivor and non-survivor groups. Accordingly, it was determined that FiO_2 , bilirubin, leukocyte, lymphocyte, and procalcitonin values statistically significantly

differed between the survivor and non-survivor groups ($p < 0.05$). The results of the receiving operating characteristics (ROC) analysis of the scoring systems for the prediction of mortality are summarized in Table 2. The highest area under the curve (AUC) was obtained from I-ROAD (0.703), while the remaining scoring systems did not have significant AUC values (<0.70) (Figure 1). A-DROP had the highest sensitivity, and CURB-65 and PSI had the highest specificity in the prediction of mortality. Table 3 shows the ROC analysis results of the duration of IMV and NIV, FiO_2 , LDH, bilirubin, WBC count, lymphocyte count, and procalcitonin, which were found to be significantly associated with mortality. According to these results, at a cut-off value of 2.5 days, the duration of invasive mechanical ventilation had the highest correlation with mortality, with an estimated AUC of 0.883.

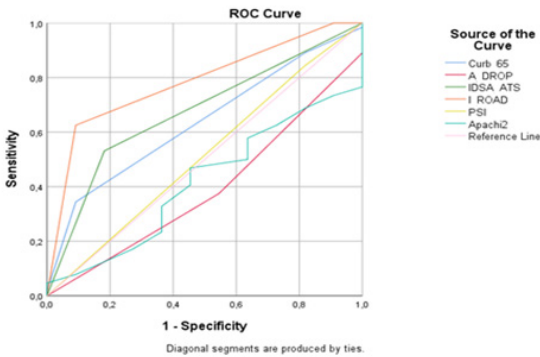


Figure 1. Area under the receiver operating characteristic curve values of different scoring systems in the prediction of 30-day mortality.

Table 1. Laboratory findings of the patients and their comparison between the survivor and non-survivor groups.

Variable	Mean (25 th -75 th percentiles)			p-value
	All patients (n = 119)	Survivors (n = 19)	Non-survivors (n = 100)	
FIO2	54.17 (40-60)	49.44 (40-55)	55.03 (50-60)	0.030 ¹
PaO ₂ /FIO ₂	171.51 (103.55-175.50)	167.80 (127.72-165.97)	172.18 (101.80-177)	0.068 ¹
GCS score	9.94 (6-14)	11.06 (9-14)	9.73 (6-14)	0.243 ¹
MAP	85.35 (76.67-94.30)	87.90 (78.35-91.08)	84.89 (76.67-91.08)	0.632 ¹
LDH	427.10 (277.5-510)	325.89 (216.75-364.75)	445.50 (291-540)	0.006 ¹
Bilirubin	0.77 (0.45-0.885)	0.56 (0.35-930.74)	0.81 (0.48-0.92)	0.050 ¹
WBC	11825.74 (7200-14550)	11224.36 (7000-12600)	15133.33 (8950-17250)	0.021 ¹
Lymphocyte	1129.25 (400-1000)	2461.11 (650-1600)	887.09 (400-900)	0.004 ¹
Hematocrit	34.42 (30.10-38.80)	33.99 (30.62-37.80)	34.50 (30-39.40)	0.808 ²
pCO ₂	43.65 (34.40-49.35)	39.27 (34.13-40.85)	44.44 (34.40-49.70)	0.090 ¹
PaO ₂	79.71 (56.10-80.55)	81.05 (57.22-72)	79.46 (56-81.10)	0.579 ¹
Lactate	2.94 (1.60-3.70)	2.00 (1.43-2.40)	3.11 (1.60-3.90)	0.060 ¹
CRP	214.47 (75-179)	110.00 (49.5-159.25)	233.46 (78-483)	0.097 ¹
Procalcitonin	112.91 (0.19-2.19)	8.97 (0.21-2.67)	684.54 (0.12-0.48)	0.023 ¹

¹Mann-Whitney U test, ²t-test; FIO₂: fraction of inspired oxygen, PaO₂: partial pressure of oxygen, GCS: Glasgow Coma Scale, LDH: lactate dehydrogenase, WBC: white blood cell, pCO₂: partial pressure of carbon dioxide, CRP: C-reactive protein, MAP: Mean arterial pressure

Table 2. Receiver operating characteristic analysis of the scoring systems for the prediction of mortality.

Scoring system	Cut-off	Youden's index	Sensitivity	Specificity	AUC
APACHE II	≤12	0.1674	0.220	0.947	0.572
CURB-65	>3	0.2947	0.400	0.894	0.639
PSI	≤4	0.0347	0.140	0.894	0.517
A-DROP	≤4	0.2189	0.640	0.578	0.605
IDSA/ATS severity criteria	>0 (no)	0.2968	0.560	0.736	0.648
I-ROAD	>2 (moderate)	0.3695	0.580	0.789	0.703

AUC: area under the curve, APACHE II: acute physiology and chronic health evaluation II, PSI: pneumonia severity index, IDSA/ATS: Infectious Diseases Society of America/American Thoracic Society

Table 3. Receiver operating characteristic analysis of variables found to be significant in terms of mortality.

Score	Cut-off	Youden's index	Sensitivity	Specificity	AUC	p-value
IMV duration	>2.5	0.7895	100.00	0.790	0.883	0.000
NIV duration	≤12.5	0.4335	0.700	0.960	0.720	0.000
FIO ₂	>40	0.2837	0.810	0.474	0.651	0.028
LDH	>353	0.3854	0.596	0.790	0.700	0.002
Bilirubin	>0.37	0.2884	0.920	0.3684	0.641	0.004
WBC	≤12,400	0.3716	0.740	0.6316	0.667	0.014
Lymphocyte	≤600	0.3395	0.550	0.7895	0.711	0.001
Procalcitonin	>0.44	0.3995	0.610	0.790	0.665	0.017

AUC: area under the curve, IMV: invasive mechanical ventilation, NIV: non-invasive ventilation, FIO₂: fraction of inspired oxygen, LDH: lactate dehydrogenase, WBC: white blood cell

Discussion

According to the results of this study, among the six pneumonia scoring systems investigated (CURB-65, PSI, A-DROP, IDSA/ATS, I-ROAD, and APACHE II), I-ROAD had the highest predictive ability for mortality in patients aged over 80 years. Another striking result of our study is that the duration of IVM and NIV, FIO₂, LDH, bilirubin, WBC count, lymphocyte count, and procalcitonin had strong correlations with mortality.

There is a strong correlation between advanced age and mortality in COVID-19 [10-12]. In a previous study, the rate of mortality was found to increase in each decade after the age of 50 years, being observed to be 2.6% in the fifth decade versus 29% in the eighth decade [13]. The high mortality rate in our study can be attributed to all patients being critically ill, old and requiring intensive care.

Respiratory failure has been one of the most typical features of COVID-19 since the beginning of the pandemic. Since COVID-19 has widespread involvement in the lungs and causes severe respiratory failure, half of the patients experience shortness of breath, and >10% require ventilator support [2]. Other studies from the literature have reported ARDS at a rate of 20-67% and mechanical ventilation and intensive care requirements at 26-32% [14]. Patients with a high oxygen demand are supported by mechanical ventilation. In the current study, in which we examined geriatric COVID-19 patients over 80 years of age, we found that the durations of IVM and NIV and FIO₂ were independent parameters associated with mortality (AUC > 0.70 for all). The duration of IMV and NIV had the highest correlations with mortality when their cut-off values were taken as >2.5 and ≤12.5 days, respectively. Based on these results, it can be predicted that mortality among patients aged over 80 will continue to increase with every passing day with no response to oxygen support in ICU.

The pneumonia guideline of the Japanese Respiratory Society recommends the use of A-DROP, CURB-65, or PSI for pneumonia in patient management [15]. In a meta-analysis evaluating these three scoring systems, the sensitivity values ranged from 60 to 69%. In our study, we obtained a similar sensitivity value only from A-DROP (64%), with CURB-65 and PSI having very low sensitivity values. This may be related to the unique physiopathology of COVID-19 and the higher mortality rate of geriatric patients than anticipated. In another study evaluating cases of nursing- and healthcare-associated pneumonia, the A-DROP, CURB-65, PSI, and I-ROAD scores were compared, and their AUC values for the prediction of 30-day mortality were reported to be 0.762, 0.808, 0.759, and 0.758, respectively [16]. These discrepancies in the literature can be due to the genetic differences of the evaluated populations. In particular, the significant difference between our study and previous studies may be related to the number of patients and the high mortality rate of our population. However, a common finding is that the I-ROAD scoring system has a high AUC value (>0.70). We found considerable differences between the scoring systems evaluated in our study. Among these scoring systems, comorbidities are only included in the calculation of PSI (malignancy, liver disease, heart failure, cerebrovascular disease, and kidney disease) and I-ROAD (malignancy and immunodeficiency). Although the relationship between comorbidities and mortality in COVID-19 has been previously clarified, this was not sufficient for PSI to be superior to the remaining scoring systems [17].

Among the blood parameters we investigated, LDH, bilirubin, WBC count, lymphocyte count, and procalcitonin were strongly correlated with mortality. Similarly, in the literature, the relationship between LDH and mortality in COVID-19 has been clearly stated [18]. In our study, LDH with a cut-off value of above 353 was found to be strongly associated with mortality

(AUC: 0.700, $p = 0.002$). Elevated bilirubin in the presence of hemolysis (AUC: 0.641) and elevated WBC especially in the presence of infection (AUC: 0.667) were also associated with a high rate of mortality in our cohort ($p = 0.004$ and $p = 0.014$, respectively). Since the beginning of the COVID-19 pandemic, lymphopenia has been one of the most important diagnostic parameters used for the prediction of mortality in COVID-19 [18]. In the current study, a lymphocyte count of ≤ 600 was associated with mortality, and lymphopenia was identified as the blood parameter that was most strongly correlated with mortality (AUC: 0.711, $p = 0.001$). This finding is supported by many studies in the literature [19,20]. Potential limitations of our study include the single-center design, the sample consisting of individuals with a similar genetic structure living in a single geographical area, and the evaluation of only intensive care patients with a high mortality rate. Multicenter prospective studies can further contribute to the literature by clearly determining mortality predictors in geriatric patients with COVID-19.

Conclusion

The early prediction of mortality due to COVID-19 pneumonia can contribute to the treatment of the disease in geriatric patients with high mortality rates. The requirement of mechanical ventilation exceeding 2.5 days can be considered the beginning of the progression to mortality in this patient population. In addition, according to the results of our study, the I-ROAD scoring system can be used to predict mortality in COVID-19 among patients over 80 who are known to have poorer survival.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Human rights

The principles set out in the Helsinki Declaration were followed. The need for informed consent was waived due to the retrospective nature of the study.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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